Center for Devices and Radiological Health

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Sousan Altaie: All right, good afternoon. I'd like to start the afternoon session with me being the speaker and having the biggest challenge in keeping every up, it's after lunch so I hope I can deliver a talk that would keep your interest and not fall asleep.

Aside from being the chairman of the educational programs, I am the Senior International Policy Analyst at the Asia Pacific office and believe it or not Canada is on my portfolio. The divisions are so that Canada has fallen within our office and we work with Canada as well in the Asia Pacific office.

My background is clinical microbiology immunology. I am a trained infectious disease specialist and spend most of my time in the coco microbiology laboratories. I still work in one aside from my FDA job.

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I started my career in academia as an assistant professor of pediatrics and directed a clinical laboratory for Children's Hospital of Buffalo, then in '95 I joined the FDA as a Primary Reviewer in the anti-infectives and then I moved on to the devices sector, became the Chief of the Immunology and Hematology Devices.

And then shortly after that I became the scientific policy advisor for the in-vitro diagnostics office and spent about 10 years there and then showed up on the Office of International Programs as a Policy Analyst.

So devices are my forte so I picked-up this talk for our Center for Devices to deliver the talk and of course our mission in CDRH is to protect and promote public health and provide a timely access to safe and effectives drugs - devices - for people.

And in addition to that we also regulate the radiation-emitting devices. Those are the lasers, the microwaves, the MRIs, all sorts of other equipment and we provide consumers, patients and caregivers with science-based information to facilitate their work as well as we facilitating the medical device innovations.

Our history of existence is grounded in a legislative mandate and these started in 1968 with the Radiation Control for Health Safety Act and then the biggest legislative that founded the Center for Devices is the Medical Devices Amendments of the 1976.

At that point the Center for Devices became a reality and grandfathered in all the devices that were already on the market and established regulatory programs based on what was already on the market.

So then the Clinical Laboratory Improvement Amendments came about and gave us the authority of classifying in-vitro diagnostic devices to be used in appropriate laboratory levels.

We have the laboratories that are divided under that CLIA rule to complex, moderately complex, and waived laboratories that are not under any sort of control so that authority came to the FDA to classify the devices we approve for the market.

Then came in 1990 Safe Medical Devices Act. Mammography Quality Standards Act came in ’92. In ’92 we also had Medical Devices Amendments

that were smaller amendments to that to kind of define the way we regulate medical devices.

In ’97 the Food and Drug Administration Modernization Act or FDAMA came about and evolved a bit more the way we regulated the devices. In 2002 the Medical Device User Fee and Modernization Act came about and kind of provided us with more timelines as far as turning around this devices into the market and that’s associated with user fees and hiring more people to do the work faster.

Then in 2005 we had Medical Devices User Fee Stabilization Act that kind of set the ground for how the fees will increase and how the performance will increase based on year after year.

In 2007, we had Food and Drug Administration Amendments Acts of 2007 which is FDAAA that had a device portion. You heard about it in the drug section but it also had a device section to it and finally in 2012 we had FDA Safety Innovation Act or FDASIA to kind of guide us in fostering device innovation.

And this is the infrastructure of the Center for Devices and Radiological Health. Jeff Shuren is the Center Director. He has two deputies, one for science and one for policy and we have a unique office called the Ombudsman Office.

The Ombudsman is responsible for direct - he’s a neutral agent - and he’s responsible to liaison between the industry who protests our decisions with the divisions who did do something that the industry didn’t like and his job is very unique and interesting because he has to work with the reviewers who let’s say declined approval of a device and an industry that is up in arms about why did you not approve my device so it’s an interesting position.

Then we have the Office of Compliance which is our post-market and premarket. Office of Compliance has two prongs to it, premarket and post-market inspections before the devices go on the market and afterwards.

And we have an Office of Device Evaluation and it regulates every device except for diagnostics, in-vitro diagnostics and the radiological diagnostic devices so basically our device review offices are only two. One is the in-vitro diagnostics and radiological diagnostic devices and one everything else.

And Office of Management is our administrative end. Office of Surveillance and Biometrics are the integral part of primary reviews because they statistically evaluate the power of the clinical trials and how effective and safe is that device.

And they also have a post-market surveillance responsibility in looking at signals for device defects that comes through the medical device reporting system. We have Office of Communication that's responsible for all the dear doctor letters or warnings about various devices that might have a problem and also advertisement and doing the webpages for us and so on and so forth.

And Office of Science and Engineering Laboratories is the research end of Center for Devices. They do regulatory-related research like say when we had (affimetrics) coming in with the chips that would diagnose lots of things.

We got them involved in doing the researching optimizing how that chip might be manufactured and so their work is just strictly regulatory-related research and help us in filling the gaps where we have regulatory shortcomes.

And CDRH is a team of 1500 dedicated skilled individuals. They are biologists, chemists, physicists, engineers, statisticians, epidemiologists,

physicians and microbiologists, nurses, pharmacists and veterinary medicine people, vets and we have toxicologists and specialists in public health education and communication.

Our communication office is a very, very active office. Our mission is always risk-benefit-based just like everywhere else in the FDA. CDRH is risk-benefit as well. We constantly juggle and balance between getting the safe and effective medical devices to the market as quickly as possible.

And while we're assuring that the medical devices currently on the market remain safe and effective and so we have in March of 2012 a guidance document that leads the industry to think about how to mitigate risk and that's a very useful guidance document for everyone to study.

And what we call a medical device has a definition embedded in the Food and Drug and Cosmetic Act and it says a device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related articles, including any component or parts of - which are accessory to the devices. And it also continues to say a medical device is intended for use in diagnosis of a disease or cure, mitigation and treatment, or prevention of a disease and they're intended to affect a structure or any function of the body of the man.

So, we do regulate - with that definition the devices that we regulate range from anywhere from a Band-Aid to a tongue depressor, to a stethoscope to a heart valves, to stents, to hip joint, to x-ray machines, MRI machines and glucometers, scissors, surgical devices. Al sorts of, pumps, and needles, and gauzes and dental amalgams. Al sorts of devices that can be drug implanted with them like the stents have a drug combination with them or the dental amalgams have drug components to them or the gauzes that we put for various

surgicals - have silver embedded in them as part - being the drug. So the variety of devices we regulate are quite vast.

Our regulatory authority comes with the 1976 Amendments and was codified in 21CFR parts 800 to 1299. And we have about 1700 devices that we currently regulate and they are within classification of 16 different specialties. And I listed them there. Their chemistry, toxicology devices, hematology/pathology devices, immunology and microbiology devices, anesthesiology - and you can read the rest of the list for your own.

So, our device classification is this risk based and it guides the amount of scientific information needed for clearing or approval of medical device for the market.

Class I devices are low-risk devices and they only require the general controls. And I will describe what the general controls are in a later slide.

Class II devices are about 800 devices that falls under their classification and they are of medium risk. We have a lot of information about them there not high risk to the patient if something goes wrong with them.

And in addition to the general controls, they require special controls and special controls can be a guidance document, can be the way these devices has to be studied for the first time, or can be a guideline about how to study this particular device or how to control it for failures.

Class III devices are of the highest risk and we have about 120 of those devices. And they need the general controls and they need pre-market approval.

And that includes giving us enough information to study the device on its own, standalone, and how it's safe and effective in performance. And it is mostly devices that need clinical trials before they go in the market.

So based on the intended use, the risk will change and the same medical device can be regulated in different classes. For example, if a medical support stocking is claiming to prevent the pooling of the blood in the legs it becomes a Class II device because the risk is higher. And if it just claims that it's a general medical purpose stocking it becomes a Class I, and it doesn't require as much regulation.

So, our regulations is risk based - is embedded in the risk to the patient and the intended use of that particular device. The intended use plays a great role in many of our regulatory pathways.

General controls I told you that were needed for all the classes of the devices are the minimum regulatory requirements for all of them. And higher classes would need more as I described to you before. So the general controls leads us to prevent a device from being adopted or misbranded and they're required to send an establishment registration. Nowadays it's not anymore on paper, it's online and electronic.

They also requires you to do device listing. A manufacturer may have many devices that they manufacture and they have to list all the devices under that particular facility that's registered.

And then they have to do a pre-market notification and that - or 510(k) for short. The 510(k) relates to the section of the - within Cosmetic Act that this particular statement was made. So in short everybody calls it 510(k) instead of pre-market notification.

And they have to comply with quality system regulations and they have to label the product and they do medical devices reporting. Those are the adverse events that happen with the devices.

I talked about special controls needed for the Class II devices and they kind of - I told you they can be guidance's and guidelines and they are mandatory performance standards. They can be recommendations or other actions that are appropriate for that particular device. They can be special labeling or they can be guidance documents. Those are the special controls I referred to that are required for Class II devices.

And the requirements for establishment registration or electronic registration of medical devices establishments, electronic or medical device listing and annual registration fee that as of 2014 is about $3313.

Please note that if establishment is overseas they also need to let the FDA know who is their agent within the United States territory.

So, to get into the labeling of the medical devices, I must say that labeling is any written material that accompanies a device or it is on the device itself. And it includes - and this labeling includes the advertisement that a device might have in the public domain. So, labeling is just not limited to the product insert but the advertisement as well.

And I talked about quality system regulations that they have to comply with. And it simply controls the design and manufacturing of medical devices.

And it's similar to ISO 13485 and also it's a standard for audits of the device establishments.

So, we have a system - a quality system regulation that doesn't tell you how to do it, but it tells you what you need to do. So, by referring to ISO standards and others - standards that are around the world -- and FDA has recognized them as recognized standards -- you actually can comply with quality system regulations that way.

The medical device reporting is equivalent to adverse event reporting in the drug sector as you heard from the previous speakers and it simply requires you to report events that led to their serious injury or malfunction of the device. And by law manufacturers and user facilities and importers of medical devices are required to do medical device reporting.

Other than that the rest of the reporting comes voluntarily through the users -- you and me and anybody -- who might have had a problem with the medical device. And these are tracked and kind of just like they are in drug they look for signals related to particular failures in a particular device and then we kind of go inspect and find cause for why the device is failing in a particular area.

So there's a lot of surveillance. That's where the Office of Surveillance comes in place and takes a look at these Medical Device Reports.

The submission types reviewed by the FDA are two kinds -- the ones that need clearance by the FDA and the ones that need approval by the FDA. The term clearance and approval have deep regulatory meanings to them. They are not casually used because the regulatory authority and the way they've been studied quite differ.

Most of the devices that are cleared are the ones that come under the 510(k) application. And about 85% to 90% of our devices come through that route of regulation by submitting a pre-market notification to us.

And the rest of the - about 20% comes under pre-market approval applications. Those are for the high risk devices that they have to stand alone in demonstrating safety and efficacy.

And then you have the Investigation Device Exemptions that are equivalent to the INDs -- Investigation New Drugs. When a device is not approved to be on the market, but you still need to study it to produce those results for approval, you request an IND - IDE which I just said is equivalent to IND.

You request an IDE, you describe what you're doing in your clinical trials and what the risk are associated. And then the FDA will approve that IND and allows you to go do your clinical trials.

The other area that needs an approval is human device exemptions. Those are equivalent to Orphan Drugs and these are orphan devices. They are only for devices that have a population less than 2000 that are affected and they need that device. So you bring it in under certain levels of study and then it gets approval for the market.

The De Novo is a very strange beast. Because our approval is - in 1976 is based on what was already on the market there are devices that there is nothing like them on the market. And when there's nothing like them under the market they can't go to the 510(k) route and they're not high risk enough to go through PMA route. So we created this administrative way of handling these devices. They're mostly Class II devices and - but because they don't have the predicates on the market they can't go through the 510(k).

We ask them to send us a pre-market notification application, work on a special control document -- which is a guidance document or a guideline or special procedures that's needed for that particular device -- and come to the FDA, say, "Here's my application. I don't have a predicate, but here's my

application." And we review it. We deny it right away. We send it back to them, say to them, "You're not substantially equivalent to a preexisting device on the market and go come back with your special controls so we can put you on the market."

And between these - and it's actually a petition that De Novo process is a petition for classifying them from a Class III device to a Class II device thereby allowing them to go on the market with less documentation or studying performance because they're not as high risk.

I hope I got that difference clear enough. And if you have questions, please ask.

So pre-market notification application is based on substantial equivalence as I said to the device that's already existing in the market. And what you need to present to us is that I'm as good as that device that already exists on the market and I am as safe and effective as that. And you simply compare yourself to another device on the market and you say I'm substantially equivalent.

So that's the framework for the 510(k).

Sometimes you don't know when the 510(k) is required. It is required when a device first time goes to the market and it is required when you make some changes to your devices to make it function better. Unfortunately or fortunately, when the drugs go on the market is one formulation - one thing doesn't change.

Devices constantly evolve, technology constantly evolves, devices - and the devices have to come back to the FDA. The ones that are already on the market they have to come back to the FDA if they have made substantial

changes to the design of the device to improve its performance to make sure it doesn't have negative impact when it's used in the hands of millions.

So, the 510(k) Program has two other kinds of applications that requires even less information to come to the FDA before they can go on the market. And those are special 510(k)'s and this use only designed controls to assure substantial equivalence to go on the market.

And then we have abbreviated 510(k)'s and these abbreviated 510(k)s are based on standards that are already existed in the public knowledge and FDA has recognized them as standards. So they come to us say, "I'm a special - I am submitting an abbreviated 510(k) because there's such and such standard that you FDA recognize as valid and I'm complying with that standard. End of story. Here's my standard that I'm complying with."

So it's a self-notification that I am complying with such a standard and they will be prone to inspection and making sure that that's what they're doing. But as far as submission, that's all they have to state. And these are usually low risk devices or changes that did not change the safety and efficacy of a particular device.

Pre-market approval, I said, are for high risk devices. And they require a pre-market application to the FDA. They usually have clinical data, clinical trial, and they have to stand on their own -- do their own clinical trials for particular indication and say, "I'm safe and effective."

And those are the highest hurdle usually. And we require them to have post-market studies afterwards if the device is really high risk.

Investigation Device Exemptions (IDE) -- I mentioned to you already -- I said, is similar to INDs when you don't have - I already discussed this so I'm going to skip it.

And as I said, Class III PMA products require post-market studies. And some of the Class II's require surveillance - post-market surveillance studies. And that's our safety nets. I addressed it when the question came up previously for drugs. It exists in the devices as well.

And we have about 17 Class II and III devices that we keep track of in the hands of the users. And these are usually implantable pacemakers -- for example -- or continuous ventilators. These are the devices - are particularly life supporting devices that if something goes wrong with them the patient dies. And so we keep a close track on those devices and how they're functioning and malfunctioning specifically to avoid disasters.

I listed the codification for various things we do. I don't think I want to go through them, but it's a good reference for you to look when you look up this 21CFR. All the parts related to the devices, those particular codifications are related to our framework of regulations. The establishments registration, the pre-market notification, and so on and so forth.

So here's a- who to contact if you need help. I am so proud of DSMICA old name and DICE the new name.

These people are on the phone 24/7. You actually can talk to a person -- an individual -- when you call that phone number. And they are very responsive in answering regulatory questions. I take pride in them. When they don't know the answer they come to the specialists into the agency and they ask and they provide you a response within 24 hours. And the director and the deputy director are really, really good friends of mine and I have a whole bunch of

faith and respect for them because they are so up on par with their regulations that there is no question they cannot answer.

So please call them if you need any information or extra help with whatever you're doing or trying to address your industry that might be importing something into the U.S. and they will respond.

And with that I want to thank you for listening to me and if you have any questions I'll be happy to respond.

Yes?

I'm sorry, I have difficulty hearing…

Man: Recently the FDA approved the marketing of the first artificial arm.

Sousan Altaie: Arm?

Man: Yes, bionic arm. And I was wondering what are the particular policies for artificial limbs or artificial organs and how are you dealing with that. Is there any particular thing you're doing for...

Sousan Altaie: When you talk about - if you're talking about artificial organs I'm sure there will be a device biologics or device drug combination.

We have an office that is called Office of Combination Products that addresses this cross - device crossed, drug crossed biologic, particular devices that come to the market. And based on the intended use of a particular device, one center takes lead and the other center become a consultative reviewer of that product.

Did I answer your question?

Man: Yes.

Sousan Altaie: Yes. Okay. So, that's how we handle it.

So the particular applicant sends their application first for designation of where I should send my device and that office handles the lead. They talk internally, they meet with the company with the two divisions that they think might be responsible for review of that product, and then they decide collectively who takes the lead, who'll be the consultative reviewer of that particular device.

Office of Combination Products.

Yes. And the Director is Thinh Nguyen. He's a (ex-deviser), a very intelligent individual. So he would be quite a good source for designation of where the device goes.

Any other questions?

Yes?

Man: I'm just curious. I would like to hear more details -- if you have -- about what happened with the morcellator, you know, it's a surgical tool - uterine surgical...

Sousan Altaie: What did you call it?

Man: Morcellator.

Sousan Altaie: I'm not familiar with the device. In fact I was reviewing some of those surgical devices just recently -- two, three years ago -- when I went on the detail in CDRH back.

Is this an incision making device or - okay.

Well, there is a series of those devices that we're kind of dealing with the regulatory aspect of how to regulate them. Some of them are radiofrequency devices, that they make the incisions, some of them are just simple lasers. Some of them are heat elements. We're still struggling with writing that guidance documents for how to regulate those. But it's in the process right now.

Man: Maybe very last question about last December the FDA shutdown the activity - asked 23andMe to stop this activity of genetic sequencing, right, because it was medical and the firm claimed it was not medical. How do you put the front tier between the project that is just entertainment or something else?

Sousan Altaie: Yes. We constantly struggle with people who don't want to be regulated and kind of changed their intended use. As I said the intended use is what determines whether you at all a medical device or not.

And we tread water and when it comes to our attention we address it. But it's a constant struggle. We constantly tweak the intended use, kind of take the words that makes them a medical device out of their intended use in those cases and - or sometimes there's no way you could take them out and they have to be regulated because of that intended use. It's a constant discussion.

Genetic sequences is also based on what you're going to use it for. If you're going to use it to kind of lead a therapy, say people who don't have this particular enzyme or short on this enzyme influences how they metabolize

certain drug, then that's diagnostic gene sequencing. It's not a wishy washy just a gene sequencing for fun. You're leading a patient management by that sequencing.

So based on that intended use of their gene sequence it can become regulated or not regulated. So we constantly kind of try to address the intended use of any sequence that might be released one point or another.